

REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at (858) 720-5133.

Status of the Claims*Pending claims*

Claims 31, 34, 35, 114, 115, 132 to 154 and 189 to 201 are pending.

These claims have been examined to the extent they are drawn to the elected species SEQ ID NO:2 and self-assembly as a way of polymerizing.

Claims added in the instant amendment

In the present response, claims 202 to 215 are added. Thus, after entry of the instant response, claims 31, 34, 35, 114, 115, 132 to 154 and 189 to 215 will be pending.

Outstanding Rejections

The rejection of claims 31, 34, 114, 115, 134, 140 to 154 and 189 to 201, under 35 U.S.C. §112, first paragraph, enablement requirement is maintained. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to methods for making a polypeptide polymer made by self-assembly of monomers, wherein at least one monomeric polypeptide of the plurality of monomeric polypeptides has a modification comprising attachment of an enzyme, attachment of a nucleotide or attachment of a nucleotide derivative or attachment of a lipid or attachment of a lipid derivative or attachment of a targeting vector, can be found, inter alia, in paragraph spanning pages 7 to 8. Claims directed to methods wherein the at least one non-monomeric polypeptide is attached to the monomeric protein as a recombinant fusion protein can be found, inter alia, on page 89, lines 12 to 14, which is paragraph [0294] of U.S. Pat. App. Pub. No. 20030198681 ("the '681

application”); see also paragraphs [0363] and [0364] of the ‘681 application. Claims directed to methods wherein the lipid comprises a polyethylene glycol can be found, inter alia, on page 89, lines 25 to 30 (which is paragraph [0296] of the ‘681 application). Claims directed to methods wherein the monomer is conjugated to an oligosaccharide can be found, inter alia, on page 90, lines 23 to 24 (which is paragraph [0300] of the ‘681 application). Claims directed to methods wherein the polymer is conjugated with a charged group can be found, inter alia, on page 110, lines 25 to 26 (which is paragraph [0362] of the ‘681 application). Claims directed to methods wherein the non-monomeric polypeptide is attached to a monomeric protein before or after polymerization can be found, inter alia, on page 89, lines 25 to 27 (which is paragraph [0296] of the ‘681 application); page 90, line 19 (which is paragraph [0300] of the ‘681 application); page 110, lines 25 to 26 (which is paragraph [0362] of the ‘681 application).

Information Disclosure Statements

Applicants thank the Examiner for noting that because no English translations of the German references (“the German theses”) were filed in the IDS of April 13, 2005, the information contained therein was not considered on the merits. The German theses are:

Mai, B.: Genetic Characterization and Expression of the Large Thermosome Subunit from *Pyrodictium occultum* in *E. coli* and Molecular Biological Studies on the Extracellular Network from *Pyrodictium abyssi* Isolate TAG11. Thesis for the Department of Microbiology at the University of Regensburg (1995).

Rieger, G.: Electron Microscope and Biochemical Studies on the Construction of the Network in *Pyrodictium*. Dissertation for the Department of Microbiology at the University of Regensburg (1998).

Schneider, S.: Electron Microscope and Protein Chemical Studies on the Structure of the Fibers and the S-Layers from *Pyrodictium occultum*. Thesis for the Department of Microbiology at the University of Regensburg (1993).

The German theses were submitted because they included portions of sequence of the cannulae proteins used to practice the methods of this claimed invention. Regarding the relevance of these theses – none of these three documents teach, suggest or speculate on uses of the cannulae proteins, nor do they teach, suggest or speculate making fusions or chimeric molecules with them.

The Schneider and Rieger theses only give partial amino-terminal (N-terminal) sequence of the cannulae proteins CanA, CanB and CanC, noting that in these references the cannulae protein sequences reported therein do not match exactly to the cannulae protein sequences described in this application, e.g., some residues in the German theses are listed as "X" or have multiple amino acids assigned to a given position – or have a different amino acid; see inter alia page 35 of the Schneider reference and page 37 of the Rieger reference.

The Mai reference discloses the entire CanA sequence - see page 44.

Accordingly, Applicants' respectfully aver that the documents as submitted in the IDS of April 13, 2005, are sufficient for the Office to consider on the record that the Schneider and Rieger theses disclose partial amino-terminal (N-terminal) sequences of the cannulae proteins CanA, CanB and CanC, and the Mai reference discloses the entire CanA sequence.

Issues under 35 U.S.C. §112, first paragraph

Enablement

The rejection of claims 31, 34, 114, 115, 134, 140 to 154 and 189 to 201, under 35 U.S.C. §112, first paragraph, enablement requirement, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention is maintained. The Office maintained this rejection based on reasons of record and further in view of argument set forth in the OA.

The Office does acknowledge that the specification is enabling for self-assembly of the peptide SEQ ID NO:2 itself.

However, it is alleged that the specification is not enabling for self-assembly of modified (by an attachment) peptide SEQ ID NO:2 and /or by substitution of its residues.

Applicants wish to clarify that the invention is drawn to methods for producing polymers by self-assembly of monomers, wherein the polymer comprises at least one monomer conjugated with a (non-monomeric) polypeptide (e.g., an enzyme, and antibody), a lipid (e.g., PEG), an oligosaccharide or a nucleic acid (e.g., a vector). It is important to note that the non-monomeric polypeptide can be attached to a monomeric protein either before or after polymerization (or both); new claims 204 and 205 clarify this point. Thus, the Office's description of the invention on page 4,

lines 9 to 12 of the OA is accurate for only one alternative embodiment of the invention – polymerization of already conjugated monomers.

Because it has been determined that the specification is enabling for methods encompassing self-polymerization of unconjugated monomers, it is reasonable to conclude that the specification is also enabling for methods for making conjugated polymers encompassing self-polymerization of unconjugated monomers with the modifications occurring only after polymerization (see new claim 204, in contrast to new claim 205).

Applicants also note that in the claimed method only one monomer in a polymer need be conjugated; see new claims 212 and 213, which clarify this point. Thus, because it has been determined that the specification is enabling for methods encompassing self-polymerization of unconjugated monomers, it is reasonable to conclude that a polymer having only one or a few conjugated monomers in a batch of many unconjugated monomers could polymerize just as efficiently as a system comprising only unconjugated monomers.

Thus, one remaining issue emphasized by the Office is whether the specification enabled polymerization of a system comprising use of only conjugated monomers or mostly conjugated monomers. To address these concerns, attached herein is a Rule 132 declaration from Dr. Nelson Barton, a co-inventor. Dr. Barton declares that one skilled in the art using the teaching of the specification could have made polymers using conjugated monomers with the exemplary protocols described, for example, in Examples 19 and 20, pages 146 to 151, of the disclosure (which are paragraphs [0540] to [0581], of the '681 application). Alternative protocols known to the skilled artisan also could have been used to self-polymerize conjugated monomers of the invention, including routine modifications of the protocols described in the specification (which would not have involved "undue experimentation") to determine. See also Dr. Barton's last Rule 132 declaration, where he declared that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art for determining conditions for self-assembly of protein conjugates of the invention was very high. Dr. Barton declared that it would have been routine for the skilled artisan at the time of the invention to screen for and select conditions that facilitated self polymerization of the claimed conjugates of the invention, whether these composition comprised monomeric polypeptides having a modification comprising attachment of an enzyme, attachment of

a nucleotide or attachment of a nucleotide derivative, or attachment of a lipid or attachment of a lipid derivative, or attachment of a targeting molecule, or attachment of a vector.

The Office also expressed concern whether conjugated monomers could successfully self-assemble into a polymer (which is more of a utility/ enablement issue, rather than a “make and use” section 112 issue, as discussed above). For example, the Office noted that it was well known that processes of self-assembly of polypeptide monomers into polymers depend critically on the structure of the monomers and even slight changes, such as change in length or chain, or additional of ionized residues, may change the rate and/or direction of the reaction (see, e.g., page 4, lines 16 to 19, of the OA).

However, Applicants respectfully aver that the specification enables the self-assemble of the conjugated monomers of the invention into a polymer, and that in fact conjugated monomers do self-associate to form polymers. In support, in the attached Rule 132 declaration Dr. Barton provides an example of a protocol describing self-assemble of exemplary conjugated monomers of the invention – monomers conjugated to an enzyme (Green Fluorescent Protein, or GFP) into a polymer. In brief, Dr. Barton describes the self-assembly of the exemplary GFP-CanA conjugated monomers of the invention, as illustrated in the attached series of fluorescence light microscope images of self-assembled GFP-CanA polymers of the invention. Thus, the specification does enable self-polymerization of only conjugated monomers or mostly conjugated monomers.

The term “Pyrotex”

The Office also expressed concerns that the term “pyrotex” was not adequately described in the specification (see, e.g., page 6, lines 15 to 19, of the OA). However, the specification clearly and expressly defines the term “pyrotex” in Figure 3A; see also page 6, lines 1 to 3 (paragraph [0337] of the ‘681 application). An applicant is entitled to be his or her own lexicographer and may rebut the presumption that claim terms are to be given their ordinary and customary meaning by clearly setting forth a definition of the term that is different from its ordinary and customary meaning(s). See MPEP §2111.01, III., page 2100-50, 8th ed. Rev. 3, Aug. 2005; In re Paulsen, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994).

Applicants also note they have used this term in public documents to refer to the polymers made by the methods of this invention; see, e.g., attached California State Science Fair document.

Exhibit A

Finally, the Office notes that the “Exhibit A” submitted with Dr. Barton’s Rule 132 declaration, dated March 24, 2005, was not readable; it appears that a photocopy (rather than a color image) of Exhibit A, an immunofluorescent light microscope image of nanotubules assembled from a polypeptide conjugate of the present invention (see page 2 of Dr. Barton’s Rule 132 declaration) was inadvertently attached in Applicants’ last response. A color image of “Exhibit A”, or the immunofluorescent light microscope image, is attached herein.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first paragraph. In view of the above, claims in this application after entry of the instant amendment are believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 564462010900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at (858) 720-5133.

Dated: June 19, 2006

Respectfully submitted,

By 

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